

It's Time to Reconsider Early-morning Testosterone Tests

Guidelines recommend collecting an early-morning sample to compensate for the natural diurnal variation in testosterone levels. But for men 45 and older, this is unnecessary.

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PRACTICE CHANGER

Early-morning testosterone tests are necessary only for men younger than 45. Because the natural diurnal variation in testosterone levels tends to diminish with age, it is acceptable to test men ages 45 and older before 2 PM.¹

STRENGTH OF RECOMMENDATION

B: Based on a retrospective cohort study.¹

ILLUSTRATIVE CASE

You are finishing up a visit with a 62-year-old man who has erectile dysfunction (ED), and you want to evaluate for androgen deficiency. It's already noon. Should you ask him to return for an early-morning visit so you can test his testosterone level?

Increasing public awareness of androgen deficiency has led to more men being tested for testosterone levels. Current Endocrine Society guidelines recommend against routine screening for androgen deficiency in men who do not have symptoms.² However, for men with classic symptoms of androgen deficiency—such as de-

creased libido, ED, infertility, depression, osteoporosis, loss of secondary sexual characteristics, or reduced muscle bulk or strength—measurement of total testosterone level is recommended.²

Due to the natural diurnal variation in serum testosterone levels, the guidelines recommend collecting the sample in the early morning.² This recommendation is based on small observational studies that included mostly men younger than 45, which found a significant difference in testosterone levels between samples drawn early in the morning and in the afternoon.³⁻⁵

In recent years, several studies have indicated that this variation declines as men age.⁴⁻⁶ Recently, researchers evaluated the effects of age and time of testing on men's total testosterone levels.

STUDY SUMMARY

Differences in testosterone levels are significant only in younger men

Welliver et al¹ performed a retrospective review of charts from a Minneapolis Veterans Affairs hospital. They identified 2,569 men seen for ED who had total testosterone levels measured between 7 AM and 2 PM in a 15-year period. Men whose total testosterone levels were outside the normal range (> 1,000 or < 50 ng/dL) or who had

total testosterone drawn after 2 PM were excluded.

The authors analyzed the results based on age, creating one group for men younger than 40 and five-year age-groups for all other men. Using scatterplot techniques, they separated each age-group into two subgroups based on draw times—7 AM to 9 AM, or 9 AM to 2 PM—and compared the mean total testosterone level for each age and time.

Participants' mean age was 63. Younger men (< 45) had the largest variation in serum total testosterone, with a large and significant decrease after 9 AM. Only the two youngest groups (ages < 40 and 40 to 44) showed a large decrease in total testosterone in specimens collected after 9 AM, compared to those drawn earlier (mean difference, 207 and 149 ng/dL, respectively). This variation was not observed in patients older than 45. Although there was a statistically significant difference between early and later testosterone levels in men ages 70 to 74, the absolute difference—34 ng/dL (452 vs 418 ng/dL)—was unlikely to be clinically significant.

WHAT'S NEW

For older men, later testing will not affect results

This study confirms previous research indicating that the diurnal

nal effect on testosterone levels becomes blunted with increasing age, at least in this group of men with ED. Allowing older men to have their total testosterone levels drawn until 2 PM would allow for greater patient flexibility in draw times, with little change in results.

CAVEATS

Study's methodology cannot account for several potential confounders

This retrospective study analyzed a single random testosterone measurement from each participant, rather than repeat testosterone levels over the course of a day. However, the study was large (2,569 men) and used mean values, which should at least partially mitigate the effect of having only a single measurement from each participant.

The study measured total testosterone and did not account for potential confounding factors—such as obesity or use of testosterone replacement therapy or androgen deprivation therapy—that could affect sex hormone binding globulin, thus potentially altering total testosterone level. However, the authors estimated that less

than 2% of the entire cohort was likely to have unrecognized hormonal manipulation with exogenous gonadotropins.

All of the men in the study were seen for ED, and it is possible that men with ED have more flattening of the diurnal variation than men without ED. However, we are unaware of other data that support this.

Up to 30% of men who have a low early-morning testosterone level may have a normal result when testing is repeated.^{2,5} Therefore, for all men who have low testosterone level test results, draw a repeat total testosterone level before 9 AM to confirm the diagnosis. Also, this study did not evaluate the course of testosterone levels throughout the later afternoon and evening, and it remains unclear whether levels can be drawn even later in the day.

CHALLENGES TO IMPLEMENTATION

Your lab's policies might require early-morning draws

There will probably be few barriers to implementing this change, unless local laboratory policies are inflexible regarding the timing of testosterone draws. **CR**

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